CLAIMS

1. Use of a GDP-L-fucose synthase protein or a protein of the RASGRP protein family, or an immunodominant fragment, immunodominant derivative or immunodominant splice variant thereof, or a nucleotide sequence encoding any of the proteins or an immunodominant fragment, immunodominant derivative or immunodominant splice variant thereof, in the manufacture of a medicament for the treatment, diagnosis and/or prevention of multiple sclerosis (MS), wherein the immunodominant fragment comprises 5 to 50, preferably 5 to 20, more preferably 10 to 15 amino acids, even more preferably 15 amino acids or the immunodominant derivative shares a homology or identity over its entire length with a corresponding part of a reference amino acid sequence of at least 75%, more preferably at least 80%, at least 85%, at least 90%, at least 93%, at least 95%, at least 97%, at least 98% or at least 99%.

2. The use according to claim 1,
wherein the GDP-L-fucose synthase protein
a) has the amino acid sequence as set forth in SEQ ID NO: 1 or
b) has an amino acid sequence which is at least 85 %, preferably at least 90 %, more preferably at least 95 % identical to the amino acid sequence as set forth in SEQ ID NO: 1 or
c) has an amino acid sequence which is at least 70 %, preferably at least 80 %, more preferably at least 90 % homologous to the amino acid sequence as set forth in SEQ ID NO: 1 or
d) has an amino acid sequence which is at least 60 %, preferably at least 70 %, more preferably at least 80 %, even more preferably at least 90 % homologous to the amino acid sequence as set forth in SEQ ID NO: 1 and the protein or immunodominant fragment or immunodominant splice variant thereof binds to an autologous HLA allele, is recognized by a T cell and/or is recognized by an antibody which binds to or recognizes the amino acid sequence as set forth in SEQ ID NO: 1 or an immunodominant fragment thereof or
e) is encoded by a TSTA3 gene, in particular by a gene sequence of nucleotides 143612618 to 143618048of NC_000008.11, or is encoded by a gene which is at least 80 %, preferably at least 90 %, even more preferably at least 95 % identical to the gene sequence of nucleotides 143612618 to 143618048 of NC_000008.11
and/or
wherein the member of the RASGRP protein family
f) has the amino acid sequence as set forth in any of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8 or SEQ ID NO: 9 or
g) has an amino acid sequence which is at least 85 %, preferably at least 90 %, more preferably at least 95 % identical to the amino acid sequence as set forth in any of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8 or SEQ ID NO: 9 or

h) has an amino acid sequence which is at least 70 %, preferably at least 80 %, more preferably at least 90 % homologous to the amino acid sequence as set forth in any of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8 or SEQ ID NO: 9 or

i) has an amino acid sequence which is at least 60 %, preferably at least 70 %, more preferably at least 80 %, even more preferably at least 90 % homologous to the amino acid sequence as set forth in any of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8 or SEQ ID NO: 9 and the protein or immunodominant fragment or immunodominant splice variant thereof binds to an autologous HLA allele, is recognized by a T cell and/or is recognized by an antibody which binds to or recognizes the respective amino acid sequence as set forth in any of SEQ ID NO: 2, SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6, SEQ ID NO: 7, SEQ ID NO: 8 or SEQ ID NO: 9 or an immunodominant fragment thereof or

j) is encoded by a RASGRP gene, in particular by a gene sequence of nucleotides

- 38488101 to 38565575 of NC_000015.10,
- 64726911 to 64745456 of NC_000011.10,
- 33436324 to 33564750 of NC_000002.12, or
- 38409051 to 38426305 of NC_000019.10,

or is encoded by a gene which is at least 80 %, preferably at least 90 %, even more preferably at least 95 % identical to the gene sequence of nucleotides

- 38488101 to 38565575 of NC_000015.10,
- 64726911 to 64745456 of NC_000011.10,
- 33436324 to 33564750 of NC_000002.12, or
- 38409051 to 38426305 of NC_000019.10.

3. The use according to claim 2, wherein the immunodominant fragment is

a) at least 85 %, preferably at least 90 %, more preferably at least 95 % identical to a respective corresponding amino acid sequence or

b) at least 70 %, preferably at least 80 %, more preferably at least 90 % homologous to a respective corresponding amino acid sequence or

c) at least 60 %, preferably at least 70 %, more preferably at least 80 %, even more

preferably at least 90 % homologous to a respective corresponding amino acid sequence and binds to an autologous HLA allele, is recognized by a T cell and/or is recognized by an antibody which binds to or recognizes the respective amino acid sequence.

4. The use according to any one of the preceding claims, wherein the immunodominant fragment comprises a sequence selected from the group comprising SEQ ID NOs: 10 to 98, preferably SEQ ID NOs: 10 to 35, preferably consists of a sequence selected from the group comprising SEQ ID NO: 10 to 98, preferably SEQ ID NOs: 10 to 35.

5. The use according to any one of the preceding claims for identifying a human subject who is suitable for tolerization to autoantigens in MS, preferably early MS, clinically isolated syndrome (CIS), radiologically isolated syndrome (RIS) or relapsing-remitting multiple sclerosis (RRMS).

6. The use according to any one of claims 1 to 4, for diagnosing pattern II MS in a human subject.

7. Use of a carrier comprising at least one protein, immunodominant fragment, immunodominant derivative, immunodominant splice variant, nucleotide sequence and/or gene sequence according to any of claims 1 to 4, in the manufacture of a medicament for the treatment, diagnosis and/or prevention of MS, wherein the carrier is coupled to the at least one protein, immunodominant fragment, immunodominant derivative and/or immunodominant splice variant, and/or the carrier contains the at least one protein, immunodominant fragment, immunodominant derivative, immunodominant splice variant, nucleotide sequence and/or gene sequence.

8. The use according to claim 7, wherein the carrier is selected from the group comprising a cell, preferably a blood cell, a protein, a lipid, a glycolipid, a bead, a nanoparticle, a virus-like-particle (VLP) and a molecule, such as a sugar molecule, and any combination thereof.

9. The use according to claim 8, wherein the protein, immunodominant fragment, immunodominant derivative and/or immunodominant splice variant is expressed by the cell, preferably the blood cell.

10. The use according to claim 8 or claim 9, wherein the blood cell is a red or white blood cell.

11. The use according to any one of claims 8 to 10, wherein the carrier is a blood cell and the blood cell is chemically coupled by a coupling agent, preferably by 1-ethyl-3-(3-dimethylaminopropyl)-carbodiimide (ECDI/EDC), to the at least one protein, immunodominant fragment, immunodominant derivative and/or immunodominant splice variant.

12. A method of manufacturing the chemically coupled blood cell of claim 11, comprising isolating the blood cell from a human subject, adding the at least one protein, immunodominant fragment, immunodominant derivative and/or immunodominant splice variant and subsequently adding the coupling agent, preferably EDC.

13. A pharmaceutical composition comprising at least one protein, immunodominant fragment, immunodominant derivative, immunodominant splice variant, nucleotide sequence and/or gene sequence according to any one of claims 1 to 4, and a pharmaceutically acceptable carrier.

14. Use of

a) at least one protein, immunodominant fragment, immunodominant derivative, immunodominant splice variant, nucleotide sequence and/or gene sequence according to any of claims 1 to 4, and/or

b) at least one carrier according to any of claims 7 to 11

in the manufacture of a medicament for inducing antigen-specific tolerance to autoantigens in a human subject suffering from or at risk of developing MS.

15. The use according to claim 14, wherein the at least one protein, immunodominant fragment, immunodominant derivative, immunodominant splice variant, nucleotide sequence and/or gene sequence is applied by nasal, inhaled, oral, subcutaneous (s.c.), intracoelomic (i.c), intramuscular (i.m.), intradermal (i.d.), transdermal (t.d.) or intravenous (i.v.) administration, preferably by i.v., s.c., i.d., t.d., oral, inhaled, nasal or coupled to a carrier, preferably a red blood cell.

16. The use according to claim 14 or claim 15, for inducing antigen-specific tolerance to autoantigens in early MS, CIS, RIS or early RRMS.

17. A method for identifying a human subject suitable for tolerization to autoantigens in MS, preferably early MS, CIS, RIS or RRMS, comprising isolating T cells and/or antibodies from blood, CSF or other body fluid of the subject and measuring reactivity of the T cells and/or antibodies against the protein, immunodominant fragment, immunodominant derivative and/or immunodominant splice variant according to any one of claims 1 to 4.